November 15, 2000

SUBJECT: Atrazine (080803) Reregistration Case No. 0062. HED Metabolism Assessment Review Committee: Residues to be Regulated and Residues of Concern for Dietary Assessment. No MRID. DP Barcode: D270177.

FROM: Catherine Eiden, Senior Scientist
Reregistration Branch 3
Health Effects Division

THRU: Steve Knizner, BSS
Reregistration Branch 3
Health Effects Division
and
Christine Olinger, Chair, MARC
Reregistration Branch 1
Health Effects Division

TO: George Kramer, Executive Secretary, MARC
Registration Branch 1
Health Effects Division

Background

The purpose of this memorandum is to document the decisions of the HED Metabolism Assessment Review Committee (MARC) concerning the following two issues related to atrazine:

1) the residues of concern for the required atrazine dietary risk assessments, and
2) the residues of atrazine to be regulated in plants, animals and in water.

These background material regarding these issues were brought before the MARC as described in HED memorandum dated 10/5/00, C. Eiden, D269513.

Members in Attendance

Members of the MARC in attendance were: George Kramer, Christine Olinger, John Doherty, William Wassel, Leung Cheng The presenting scientists were: Catherine Eiden (HED), Roger Hawks (HED), Steve Knizner (HED), Mary Frankenberry (EFED), Jim Lin (EFED).

Summary of Deliberations and Decisions

Issue 1: Residues of Concern for Dietary Risk Assessments

Questions to the Committee

Based on what is now known about the specific mechanism of toxicity by which atrazine acts, does the Committee still consider a separate dietary risk assessment based on the endpoints for atrazine necessary for total radioactive residues minus free hydroxy compounds?

MARC Decision

The MARC determined that based on current toxicological endpoints established for atrazine and its chloro-metabolites and separate toxicological endpoints established for hydroxy-atrazine, a risk assessments is not required for "total radioactive residues minus free hydroxy compounds". This decision was based on the fact that the chronic RfD for atrazine is based on hormonal effects resulting in the LH surge in Sprague Dawley rats, which is a cancer precursor effect for this strain of rats. The weight of the evidence for triazines indicates that a chlorine constituent must be present on the triazole ring in order to elicit this cancer precursor effect. Thus, nonchlorinated triazines are not of toxicological concern in relation to the atrazine toxicological endpoints.

Issue 2: Residues to be Regulated in Plants, Animals, and Water

Tolerances are established for residues of the herbicide atrazine, 2-chloro-4-ethylamino-6-isopropylamino-s-triazine, in or on agricultural plant and animal commodities (40 CFR 180.220(a)(1) [corn, sorghum, wheat, sugarcane, rye grass, guava, macadamia nuts, meat/milk/poultry/eggs], and under 40 CFR 180.220(a)(2) for combined residues of atrazine and its metabolites 2-amino-4-chloro-6-ethylamino-s-triazine (G-28279), 2-amino-4-chloro-6-isopropylamino-s-triazine (G-30033), and 2-chloro-4,6-diamino-s-triazine (G-28273), (40 CFR 180.220(b)) [range grass and orchard grass, and hay].

Questions to the Committee

Based on the information presented as to the metabolism of atrazine in plants, does the Committee recommend that the residues to be regulated in plants to be atrazine, *per se* as in 180.220(a)(1) or as atrazine and the chloro-metabolites as in 180.220(a)(2)?

Based on the information presented on the metabolism of atrazine in animals, and the

predominance of the chlorinated compounds in animal tissues and milk, does the Committee recommend that the residues to be regulated in animals are atrazine and the chloro-metabolites?

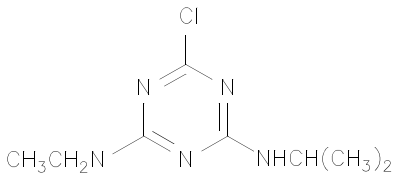
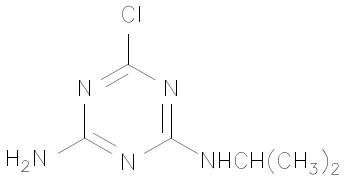
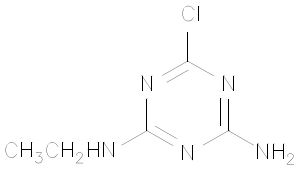
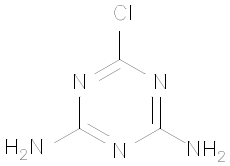
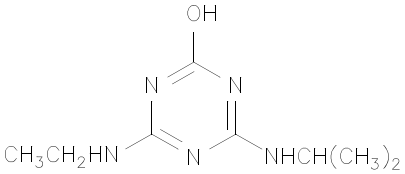
Based on the information presented on the degradation of atrazine in water, does the Committee agree that the residues to be included in risk assessment for water exposure are atrazine and the chloro-metabolites?

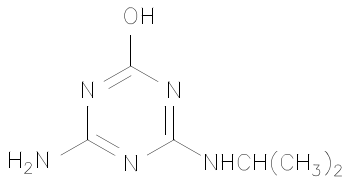
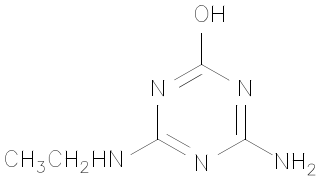
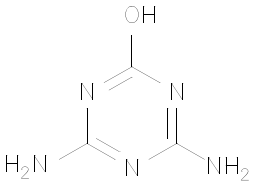
MARC Decision

The HED MARC determined that residues of atrazine and the chloro-metabolites should be regulated in both plants and animals because the chloro-metabolites are present in detectable quantities in animal feeds (forages and stover) and do transfer to the meat and milk of ruminants through these feeds. The MARC further concluded that because the hydroxy metabolites of atrazine are the major plant metabolite and are present in detectable quantities in feeds, the four hydroxy metabolites of atrazine should be regulated in plants and animals, as well. For the purposes of drinking water risk assessment, the MARC concluded that the compounds of concern were the atrazine and chloro-metabolites.

HED recommends establishing tolerances under 40 CFR 180.220 (a)(1) for the combined residues of atrazine and its metabolites 2-amino-4-chloro-6-ethylamino-s-triazine (G-28279), 2-amino-4-chloro-6-isopropylamino-s-triazine (G-30033), and 2-chloro-4,6-diamino-s-triazine (G-28273) [corn, sorghum, wheat, sugarcane, rye grass, range grass, guava, macadamia nuts, ruminant meat and milk]. HED recommends establishing separate tolerances under 40 CFR 180.220(a)(2) for combined residues of 2-hydroxy-4-ethylamino-6-isopropylamino-s-triazine (G-34048), 2-amino-4-hydroxy-6-isopropylamino-s-triazine (GS-17794), 2-amino-4-hydroxy-6-ethylamino-s-triazine (GS-17792), and 2,4-diamino-6-hydroxy-s-triazine (GS-17791) [corn, sorghum, wheat, sugarcane, rye grass, range grass, guava, macadamia nuts].

As a practical consideration, HED is recommending for separate tolerances for atrazine's hydroxy metabolites rather than combining all atrazine residues, because the toxic endpoints established for the hydroxyatrazine compounds are different from the toxic endpoints established for atrazine and the chloro-metabolites. All dietary risk assessments conducted for atrazine will necessarily be conducted on two sets of residues: 1) exposures to the four hydroxy metabolites compared to specific endpoints for hydroxyatrazine, and 2) exposures to atrazine and the chloro-metabolites compared to specific endpoints for atrazine. The chemical structures of the residues to be regulated are given below. The HED Residue Chemistry Chapter (11/15/00) contains the relevant information regarding the residues to be regulated for atrazine, new tolerance expressions, and the establishment of any new tolerances.

Common/Chemical Name (Code)	Chemical Structure
Atrazine 2-chloro-4-ethylamino-6-isopropylamino-*s*-triazine (G-30027)	
2-amino-4-chloro-6-isopropylamino-*s*-triazine (G-30033)	
2-amino-4-chloro-6-ethylamino-*s*-triazine (G-28279)	
2,4-diamino-6-chloro-*s*-triazine (G-28273)	
Hydroxyatrazine 2-hydroxy-4-ethylamino-6-isopropylamino-*s*-triazine (G-34048)	

Common/Chemical Name (Code)	Chemical Structure
2-amino-4-hydroxy-6-isopropylamino-*s*-triazine (GS-17794)	
2-amino-4-hydroxy-6-ethylamino-*s*-triazine (GS-17792)	
Ammeline 2,4-Diamino-6-hydroxy-*s*-triazine (GS-17791)	

CAE, 824B, 305-7887, 10/26/00
SAK, 821, 10/26/00